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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,432	12/30/2003	Charles R. Roe	BHCS:1006RCE	7856

34725 7590 05/12/2009
CHALKER FLORES, LLP
2711 LBJ FRWY
Suite 1036
DALLAS, TX 75234

EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
05/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,432	ROE, CHARLES R.	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,21-30 and 32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,21-30 and 32-37* is/are rejected.

7)☒ Claim(s) *28 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/06/2009 has been entered.

2. Applicant's response, filed 4/06/2009, to the Office Action mailed 1/05/2009 is acknowledged. Applicant amended Claims 15, 21-23, 30, 32, 35, and 36, canceled Claims 16, 17, and 31, added Claim 37, and presented arguments in response to the Office Action.

3. Claims 15, 21-30, and 32-37 are pending and presently under consideration.

4. Applicant's arguments have been fully considered and are persuasive in part. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

5. Applicant has amended Claim 28 in an attempt to overcome the objection of the claim (inappropriate period (".") between the words "provided" and "parenterally") in the

previous Office Action. Applicant apparently tried to strike-through the period, but instead entered "÷". The deletion of the "÷" In the presently amended claim should be signified by the use of double brackets (i.e., [[÷]]). Appropriate correction is required.

6. Claim 37 is objected to because of the following informalities: The claim recites "a nutritionally_effective". The "_" between "nutritionally" and "effective" should be replaced with a space. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

Applicant's Specification does not support the recitation by Claim 37 of "A method for suppressing the effects of translocase deficiency of a human infant, consisting essentially of: identifying a human infant suspected of having a translocase deficiency; [and] administering to said infant a nutritionally effective amount of a compound selected from…" (emphasis added). The Specification does not disclose or provide guidance as to what would materially affect the basic and novel characteristics

of the claim and thus, what would be excluded by the "consisting essentially of" language of the new claim.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 15, 21-30, and 32-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odle et al. (Journal of Nutrition, 1991, Vol. 121, pages 605-614; provided by Applicant), in view of Ajinomoto (JP 52015834A (provided by Applicant)) and Jandacek et al. (US Patent No. 4,753,963), further in view of Kerner et al., ("Genetic Disorders of Carnitine Metabolism and Their Nutritional Management", in Annual Review of Nutrition, 1998, Vol. 18, pages 179-206, previously presented) .

Inhibition of mitochondrial β-oxidation of long-chain fatty acids, and its physiological effects, caused by a deficiency of acylcarnitine/carnitine translocase is well known by one of ordinary skill in the art, as is a test for acylcarnitine-carnitine translocase activity used in diagnosis of the deficiency, as taught by Kerner et al. See pages 192-193. Kerner et al. teach "[t]he disease shows autosomal recessive inheritance with very early onset and lethal outcome in the perinatal and early infantile period of life." See page 193. Therefore, neonatal and premature infants would obviously benefit from a treatment for the disease.

Odle et al. teach that changes in chain length within the medium-chain fatty acid family "may dramatically influence the rate and extent of digestion and/or absorption and metabolism of medium-chain triglycerides by neonates". One of the benefits of the medium-chain fatty acids is their "preferential oxidation because of less dependence on carnitine acyltransferase/translocase system for entry into the mitochondria". See abstract and 1st paragraph, page 605. Odle et al. disclose studies of medium-chain triglycerides containing unsaturated 7, 8, 9, and 10 carbon fatty acids. The reference suggests propionyl-CoA arising from the β-oxidation of odd-carbon fatty acid triglycerides (7 carbon more pronounced than 9 carbon) could diminish the hyperketonemia associated with medium-chain triglycerides. See 1st 11 lines, left column, page 606; and the 1st half of the right column, page 612.

One of ordinary skill in the art would have found it obvious to utilize the teachings of Odle et al. to provide to individuals suffering from acylcarnitine/carnitine translocase deficiency more readily absorbed and metabolized fats (i.e., triglycerides of medium chain fatty acids, particularly 7 and 9 carbon-chain fatty acids, such as "tri-7:0", a triglyceride of heptanoic acid (triheptanoin)).

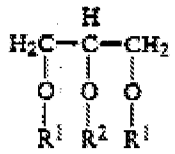
Ajinomoto teaches an oral (enteral) triheptanoin nutritional supplement that includes triheptanoin alone, or in combination with proteins, oils, carbohydrates, vitamins and minerals. The triheptanoin comprised ≥ 30 wt% of the total weight of the supplement. The supplement can include a beverage, such as milk. The reference discloses the composition is readily absorbed from the digestive system to supply calories without participation of insulin (insulin sensitivity is frequently diminished in

premature infants) and without producing excess ketones (also taught by Odle et al., *supra*).

Triheptanoin is metabolized by the body (via lipolysis) to glycerol and three molecules of heptanoic acid. Therefore, administration of a composition comprising triheptanoin is equivalent to administration of a composition comprising heptanoic acid, as required by instant Claim 15. Indeed, the instant Specification (paragraph 70) discloses the "terms heptanoic acid, heptanoate, and triheptanoin may be used interchangeably".

The cited references do not teach specific dosages of triheptanoin, heptanoic acid, or other 7 carbon-chain fatty acids.

Jandacek et al. discloses a nutritional fat suitable for enteral and parenteral products (see abstract). The fat disclosed by Jandacek et al. consists of triglycerides having the following formula:



wherein each R^1 group is selected from n-heptanoyl, n-octanoyl, n-nonanoyl, n-decanoyl and n-undecanoyl groups; and the R^2 groups comprise from 0 to about 90% saturated acyl groups selected from n-heptanoyl, n-octanoyl, n-nonanoyl, n-decanoyl, n-undecanoyl, lauroyl, myristoyl, palmitoyl, stearoyl and mixtures thereof; from 0 to about 90% oleoyl groups; from about 10 to 100% linoleoyl groups; and from 0 to about 10% linolenoyl groups.

When R1 and R2 are selected to be n-heptanoyl, this formula results in a nutritional fat compound that is identical to triheptanoin.

The reference is drawn to developing a nutritional fat in a form which is well absorbed by those persons such as infants which have fat malabsorption problems (column 1, lines 45-48). Jandacek et al. teaches enteral compositions comprising the nutritional fat (triglycerides) disclosed in the reference, a source of carbohydrates, a source of amino acids and optionally, components such as vitamins and minerals. The composition can be formulated as a dry mixture or mixed with water to provide a fluid formulation for enteral administration. See column 5, lines 1-9. The amount of the triglyceride utilized in the composition is a *nutritionally effective amount*, based upon the subject and the nutritional benefits required. The composition typically comprises the nutritional fat (triglyceride) in an amount of about 2% to about 20% by weight of the composition (about 18 to about 180 calories per 100 grams of composition or about 4% to about 36% of the total caloric value of the composition). See column 5, lines 18-20 and column 7, lines 5-8. The reference discloses oral and feeding tube administration of the composition. See column 4, last paragraph. Jandacek et al. also discloses parenterally administrable compositions. See column 6, lines 56-60).

As discussed *supra*, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the teachings of Odle et al., which suggest enhanced β-oxidation of odd-carbon fatty acid triglycerides (especially 7 carbon fatty acid triglycerides), to provide to individuals suffering from acylcarnitine/carnitine translocase deficiency (including in prematurely-born human infants) more readily

absorbed and metabolized fats. The artisan would have been motivated to find suitable compositions taught in the art. Ajinomoto teaches such a composition (triheptanoin) and further discloses its use as a suitable source of easily absorbed (fat derived) calories that do not require insulin for absorption (as would be required by a carbohydrate derived source of calories). These two references would have motivated the artisan to utilize the teachings of Jandacek et al., selecting a triglyceride comprised of 3 n-heptanoyl groups (i.e., triheptanoin). Jandacek et al. teaches compositions of triglycerides, disclosing concentration ranges for the triglycerides of said compositions (*supra*). It is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(11). One of ordinary skill in the art would have adjusted triheptanoin concentrations and dosage schedules as appropriate, based upon factors such as, the age and weight of the patient, the severity of the condition being treated and the route of administration.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of

ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant argues "[t]he combination of references fails to teach each and every limitation of the instant invention. Specifically, the combination fails to disclose a method of suppressing the effects of translocase deficiency of a prematurely-born human infant by identifying an infant suspected of having a translocase deficiency; and administering to an infant suspected of having a translocase deficiency a composition comprising a nutritionally effective amount of a n-heptanoic acid to treat the translocase deficiency.

Specifically, Applicant argues "Odle fails to teach a method of suppressing the effects of translocase deficiency of a prematurely-born human infant. Odle fails to disclose administering to said human infant a nutritionally effective amount of a compound. Odle fails to disclose identifying an infant suspected of having a translocase deficiency. Odle fails to disclose administering to an infant suspected of having a translocase deficiency a composition. There is NOTHING in Odle that relates to the treatment of humans having a translocase deficiency. There is nothing in Odle that indicates that a seven-carbon fatty acid is safe for consumption by humans or has any particular nutritional benefit to humans.

As presented supra, Kerner et al., inhibition of mitochondrial β-oxidation of long-chain fatty acids, and its physiological effects, caused by a deficiency of acylcarnitine/carnitine translocase is well known by one of ordinary skill in the art, as is

a test for acylcarnitine-carnitine translocase activity used in diagnosis of the deficiency. Further, Kerner et al. teach "[t]he disease shows autosomal recessive inheritance with very early onset and lethal outcome in the perinatal and early infantile period of life." Therefore, neonatal and premature infants would obviously benefit from a treatment for the disease, thus providing motivation to apply the teachings of Odle et al., i.e., administration of medium-chain triglycerides (particularly triglycerides of 7 carbon-chain fatty acids) to treat carnitine acyltransferase/translocase deficiency in neonatal pigs. It would have been obvious to one of ordinary skill in the art to apply teachings of nutrition (e.g., dietary supplements, nutraceuticals and functional foods), derived from experiments with pigs, directly to humans. This is evidenced by the disclosure of the review article of Miller et al. ("The Pig as a Model for Human Nutrition", 1987, Annual Review of Nutrition, Vol. 7, pages 361-382). For example, Miller et al. teach pig and human nutrient requirements are similar in more ways than any other nonprimate mammalian species, providing a basis for the use of the pig in many human nutritional studies. See page 363, 4th paragraph.

Applicant argues that while Ajinomoto may disclose a food having triheptanoin, "Ajinomoto states that the additives [(triheptanoin)] are not necessarily pure e.g. may contain a small amount of fatty acids". Further, Applicant argues Ajinomoto discloses but fails to enable a food composition having triheptanoin.

The argument that the triheptanoin taught by Ajinomoto is "not necessarily pure" is confusing since this is not required by the instant claims. Additionally, the instant

claims are not drawn to a method of making triheptanoin or any other agent or composition.

Applicant argues "Jandacek fails to disclose administering to said human infant a nutritionally effective amount of a compound. Jandacek does not disclose identifying an infant suspected of having a translocase deficiency nor does Jandacek disclose the administering to an infant suspected of having a translocase deficiency a composition comprising a seven carbon fatty acid selected from triheptanoin or n-heptanoic acid or derivatives thereof [(it is noted that the instant claims do not recite derivatives of triheptanoin or n-heptanoic acid)]. As such, the combination still fails to teach each and every limitation."

One cannot show nonobviousness by attacking references individually where the rejection is based on combinations of references. The reference to Jandacek et al. is part of a rejection under 35 U.S.C. 103(a) and is provided to demonstrate prior art knowledge of fats (which can include triheptanoin) suitable for enteral and parenteral products.

Applicant asserts "it is improper to combine Jandacek with Odle and Ajinomoto since Jandacek is at the very most non-enabling art. Jandacek is not enabling art because it is merely a broad listing of possible different compounds does not place seven carbon fatty acid selected from triheptanoin or n-heptanoic acid or derivatives thereof in possession of the public."

Although the listing of potentially useful compounds by Jandacek may be considered broad, the teachings of Odle et al. and Ajinomoto would have motivated the

artisan to select triglycerides of 7 carbon fatty acids and in particular triheptanoin (taught by Ajinomoto).

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12.

13. Claims 15, 21-30, and 32-37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4 of U.S. Patent No. 6,740,679 B1, in view of Kerner et al. (cited above). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to treating patients having translocase deficiency with 7 carbon fatty acids.

Inhibition of mitochondrial β-oxidation of long-chain fatty acids, and its physiological effects, caused by a deficiency of acylcarnitine/carnitine translocase is well known by one of ordinary skill in the art, as is a test for acylcarnitine-carnitine translocase activity used in diagnosis of the deficiency, as taught by Kerner et al. (*supra*). Kerner et al. teach "[t]he disease shows autosomal recessive inheritance with very early onset and lethal outcome in the perinatal and early infantile period of life." Therefore, neonatal and premature infants would obviously benefit from a treatment for the disease.

Although the conflicting claims are not specifically drawn to treating infants or to identifying an infant suspected of having a translocase deficiency, in view of Kerner et al., said infants would be encompassed by the conflicting claims recitation of treatment of a patient having an inherited or acquired deficiency in at least one enzyme involved in fatty acid metabolism (specifically, carnitine/acylcaritine translocase) and the implied step of first identifying said patients.

Conclusion

14. Claims 15, 21-30, and 32-37 are rejected.

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is

(571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614